

American Heart Association Tobacco Regulation and Addiction Center (A-TRAC)

Cardiovascular Injury Due to Tobacco Use (Project 2)

Bhatnagar, Aruni

P50 HL-120163-01

Abstract:

The overall goal of this project is to understand the cardiovascular effects of tobacco use in humans. We will assess whether the biomarkers of cardiovascular injury identified in Project 1 in mice also reflect tobacco-induced cardiovascular damage (TICD) in humans, and if they are predictive of subclinical cardiovascular disease and major cardiovascular clinical events. The identification of biomarkers reflective of TICD and their relationship to the biomarkers of tobacco exposure will be critical in assessing which constituents of tobacco smoke and smokeless tobacco impact cardiovascular toxicity and how the cardiovascular effects of HPHC could be measured. Specific Aims include: 1. To elucidate the relationship between biomarkers of cardiovascular dysfunction/injury and specific measures of exposure to tobacco smoke and smokeless tobacco. To identify indices of cardiovascular injury, biomarkers of endothelial damage and predilection for thrombosis will be evaluated in a cohort of 480 smokers, ST users, and non-smokers without overt CVD. The project team will determine how these biomarkers are associated with the extent and duration of exposure to nicotine and other tobacco constituents such as reactive aldehydes. To assess injury, they will measure endothelial vasodilator function (flow-mediated dilation), arterial stiffness (pulse wave velocity), endothelium-derived microparticles; endothelial progenitor cells (EPCs), and changes in thrombosis. Exposure will be evaluated by measuring the urinary metabolites of nicotine and tobacco and tobacco-smoke derived aldehydes. 2. To identify and compare the dose-dependent associations between tobacco exposure, measures of subclinical cardiovascular disease, and clinical cardiovascular events. Using data from the Multi-Ethnic Study of Atherosclerosis (MESA) prospective cohort, we will examine cross sectional associations between tobacco exposure and subclinical vascular disease as assessed by carotid intima-media thickness (cIMT), coronary artery calcification (CAC), ankle brachial index (ABI), flow-mediated dilation and arterial stiffening, and biomarkers of inflammation. 3. To validate candidate biomarkers associated with tobacco exposure in independent human cohorts. Candidate bio-markers reflective of tobacco-induced cardiovascular injury, identified in Aims 1 and 2 will be independently validated in The Jackson Heart Study (JHS) cohort and in HCHS-SOL and assessed for their association with urinary metabolites of nicotine and aldehydes. This project will lead to the identification and validation of novel biomarkers of endothelial injury that are associated with exposure to tobacco and tobacco constituents. The study results will assess which tobacco-associated biomarkers of injury reflect the extent and the progression of cardiovascular disease and what magnitude of changes in these biomarkers translates into meaningful impacts on CVD outcomes.